Attorney's Docket No. 18.006011 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Hickok, *et al.*		
Assignee:	CYTYC Corporation	Confirmation No.	8562
Filing Date:	February 6, 2004	Examiner:	Grun, James Leslie
Serial No.:	10/774,144	Group Art Unit:	1641
Title:	Screening and Treatment Methods for Prevention of Preterm Delivery		

MAIL STOP APPEAL BRIEF-PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDED APPEAL BRIEF

Sir:

This Amended Appeal Brief is filed in response to the Notification of Non-Compliant Appeal Brief mailed February 23, 2009 and pursuant to the "Notice of Appeal to the Board of Patent Appeals and Interferences" filed December 12, 2008. In the Notice of Non-Compliance, the Examiner argues that the Grounds of Rejection is not consistent with the Office Action mailed July 29, 2008. The Grounds of Rejection section as well as the Status of the Claims, Grouping of the Claims and the Argument (Issue 4) sections have been amended to recite all of the claims rejected under 35 U.S.C. § 103(a). The Appellant requests that the following amended brief be entered in its entirety.

Real Party in Interest.

The real party in interest in this appeal is Cytyc Corporation, Inc., the assignee of the above-referenced patent application.

Related Appeals and Interferences.

There are no related appeals and/or interferences involving this application or its subject matter.

Status of Claims.

Claims 67-94 are the subject of this appeal.

Claims **67-76, 79,** and **81-94** are rejected under 35 U.S.C. §112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention.

Claims **67-94** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims **67-94** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims **67-76 and 79-94** are rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt *et al.* (WO 94/17405) in view of Johnson *et al.* (NEJM 293: 675, 1975), Meis *et al.* (Am. J.

Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner *et al.* or Anderson *et al.*

Claims 77 and 78 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt *et al.* (WO 94/17405) in view of Johnson *et al.* (NEJM 293: 675, 1975), Meis *et al.* (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner *et al.* or Anderson *et al.* and in further view of Allen *et al.* (Exp. Biol. Med. 226:498, 2001) or Olsen *et al.* (Lancet 339: 1003, 1992).

The pending claims under appeal appear in Appendix A. No other claims are pending. Claims 1-66 have been cancelled.

Status of Amendments.

Appellant's Amendment After Final filed November 11, 2008 was not entered by the Examiner.

Summary of the Claimed Subject Matter.

The Appellant's pending claims of the present invention are directed to a method for screening and treating a subject, comprising: a) obtaining a sample from a subject who is asymptomatic for preterm or imminent delivery; b) detecting a fetal restricted antigen in said sample from said subject and assessing whether the level of fetal restricted antigen is indicative of a risk of preterm or imminent delivery; and c) if the level of fetal restricted antigen is indicative of the risk, administering a progestational agent to the subject, whereby delivery is delayed.

A summary of the claimed subject matter defined in independent claim 1 involved in the Appeal may be found in paragraphs [0084] to [0089] and in paragraphs [0121] to[0157] of the specification as well as Examples 9, 10, and 11.

Grounds of Rejection to be Reviewed on Appeal.

Whether claims 67-76, 79, and 81-94 are properly rejected under 35 U.S.C. §112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention.

Whether claims 67-94 are properly rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Whether claims 67-94 are properly rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Whether claims 67-76 and 79-94 are properly rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt *et al.* (WO 94/17405) in view of Johnson *et al.* (NEJM 293: 675, 1975), Meis *et al.* (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner *et al.* or Anderson *et al.*

Whether claims 77 and 78 are properly rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt *et al.* (WO 94/17405) in view of Johnson *et al.* (NEJM 293: 675, 1975),

Meis *et al.* (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner *et al.* or Anderson *et al.* and in further view of Allen *et al.* (Exp. Biol. Med. 226:498, 2001) or Olsen *et al.* (Lancet 339: 1003, 1992).

Grouping of Claims.

The claims do not stand or fall together

Claims 67-94 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 67-94 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 67-76 and 79-94 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt *et al.* (WO 94/17405) in view of Johnson *et al.* (NEJM 293: 675, 1975), Meis *et al.* (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner *et al.* or Anderson *et al.* Claims 77 and 78 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt *et al.* (WO 94/17405) in view of Johnson *et al.* (NEJM 293: 675, 1975), Meis *et al.* (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner *et al.* or Anderson *et al.* and in further view of Allen *et al.* (Exp. Biol. Med. 226:498, 2001) or Olsen *et al.* (Lancet 339: 1003, 1992). Accordingly, the issues surrounding the claims are different, and the claims do not stand or fall together.

ARGUMENT

Issue 1-- Whether claims 67-76, 79, and 81-94 are unpatentable under 35 U.S.C. 112, first paragraph for failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention.

The statutory basis of the written description requirement under 35 U.S.C. § 112, first paragraph requires that the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same.

Claims 67-76, 79, and 81-94 remain rejected 35 U.S.C. 112, first paragraph as containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In the Final Office Action dated July 29, 2008, the Examiner rejected the Appellants' claims, arguing that the ability to prolong a pregnancy at risk for preterm delivery is not known or common to the list of progestational agents disclosed by the Appellants. This is an inappropriate rejection under 35 U.S.C. 112, first paragraph.

A patent application complies with the written description requirement under 35 U.S.C. § 112, first paragraph simply "by describing the invention, with all of the claim limitations." *Lockwood v American Airlines, Inc.* 107 F.3d 1565, 41 USPQ2d 1961, 1966 (Fed.Cir. 1997). The argument that

the list of progestational agents provided by the Appellant are not known to have the ability to prolong a pregnancy at risk for preterm delivery is not supported by any facts provided by the Examiner and irrelevant to the issue of written description. To satisfy the written description requirement, all the Appellants need to demonstrate is that the application reasonably describes or conveys to one of ordinary skill in the art at the time the patent application was filed, that the Appellants had possession of the method described in independent claim 67 (as well as claims 68-76, 79, and 81-94 which depend therefrom). Since all of the method steps are described and supported by the specification, the written description requirement is satisfied. The Examiner appears to be making an enablement argument which is better addressed under 35 U.S.C. 112, second paragraph.[1] Because the method of the present invention is clearly set forth in claim 67, the Appellants respectfully assert that a sufficient description of the current invention has been shown and respectfully requests that the rejection under 35 U.S.C. §112, first paragraph be reversed.

Even assuming *arguendo* that the Examiner rejected claims 67-76, 79, and 81-94 under 35 U.S.C. § 112 first paragraph for lack of enablement, the Examiner's argument cannot stand due to the fact that the Examiner admits that there are at least two functional examples of pregnancy prolonging agents described in the Appellants' specification .

Issue 2-- Whether claims 67-94 are unpatentable under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The statutory basis of the written description requirement under 35 U.S.C. § 112, first paragraph requires that the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same.

Claims 67-94 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.. Specifically, the in Final Office Action, the Examiner asserted that "...the Applicant does not define, and one would not readily know absent further guidance from applicant, what patients are encompassed by the current criteria of 'asymptomatic'."(Page 4) The Examiner went on to further argue that even though any pregnant patient is contemplated by the invention "...such possibility of use does not provide explicit or implicit indication to one of skill in the art that only 'asymptomatic' patients were originally contemplated as part of applicant's invention..." The Appellants respectfully disagree.

In the background section of the specification (paragraph [0003]), the Appellants state that "...due to the subtlety of symptoms associated with preterm delivery, many subjects are not

diagnosed as having an increased risk of preterm delivery until later in their pregnancies." (Emphasis added) It is clear that the Appellants contemplated that the lack of symptoms (i.e., being asymptomatic) is a significant problem associated with preterm delivery. In paragraph [0085] of the specification, the Appellants specifically point what some of those symptoms may be by teaching that "...there are a large number of factors known to be associated with the risk of preterm delivery. Those factors include, but are not limited to, multiple fetus gestations; incomplete cervix; uterine anomalies; polyhydramnios; nulliparity; previous preterm rupture of membranes or preterm labor; preeclampsia; first trimester vaginal bleeding; little or no antenatal care; and symptoms such as abdominal pain, low backache, passage of cervical mucus and contractions." (Emphasis added). Thus, it is clear that the Appellants contemplated the issue of women who are asymptomatic of preterm delivery but who are still at risk of giving birth to a premature infant. The Appellants respectfully asserts that the term "asymptomatic" is not new matter and respectfully requests that the rejection under 35 U.S.C. §112, first paragraph be reversed.

Issue 3-- Whether claims 67-94 are properly rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 67-94 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Appellants regard as the invention. In the Amendment after Final submitted November 11, 2008, the Appellants amended claims 67, 68, 71, 75, 80, 81, 83, 85, 86, 87, 91 and 92 to correct antecedent basis. The Examiner rejected this amendment, citing the fact that the proposed claim amendments did not place the application in better form for appeal by simplifying the issues for appeal, which is clearly not true. The Appellants respectfully request that the claim amendments submitted in the Amendment after Final filed November 11, 2008 be entered and the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

Issue 4-- Whether claims 67-76 and 79-94 are properly rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt et al. (WO 94/17405) in view of Johnson et al. (NEJM 293: 675, 1975), Meis et al. (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner et al. or Anderson et al.

Claims 67-76 and 79-94 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt *et al.* (WO 94/17405) in view of Johnson *et al.* (NEJM 293: 675, 1975), Meis *et al.* (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner *et al.* or Anderson *et al.* This rejection is respectfully traversed.

In the Final Office Action, the Examiner argued that "...it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have tested a pregnant patient determined to have biochemical markers indicative of impending preterm delivery for the status of the fetal membranes and to treat those patients with intact fetal membranes indicated as at risk of having impending delivery with a pregnancy-prolonging agent because of the direct suggestion in Leavitt *et al.* to do so" The Appellants respectfully disagree with the Examiner that Leavitt *et al.* in view of Johnson *et al.*, Meis *et al.*, or Keirse and in further view of Weiner *et al.* or Anderson *et al.* teach or suggest either alone or in combination, a method of screening and treating a subject who is asymptomatic for preterm or imminent delivery by administering a progestational agent as described in independent claim 67.

To properly establish a *prima facie* case of obviousness of a claim under 35 U.S.C. §103(a), all the claim limitations must be taught or suggested by the prior art, and all words in a claim must be considered in judging the patentability of that claim against the prior art. MPEP §2143.03. In the

present case, independent Claim 67 (from which dependent claims 68-76 and 79-94 depend) requires the express limitation of "...obtaining a sample from a subject who is asymptomatic for preterm or imminent delivery..." Nowhere in Leavitt *et al.*, Johnson *et al.*, Meis *et al.*, Keirse, Weiner *et al.* or Anderson *et al.*, either alone or in combination, is there any teaching or suggestion of testing and treating an asymptomatic patient. Without this teaching, the references cited by the Examiner are insufficient to show obviousness. Therefore, Applicant respectfully submits that claims 67-76 and 79-94 are patentable over the cited references. The Appellants respectfully requests that the rejection of claims 67-76 and 79-94 under 35 U.S.C. §103, be reversed.

Issue 5— Whether claims 77 and 78 are properly rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt et al. (WO 94/17405) in view of Johnson et al. (NEJM 293: 675, 1975), Meis et al. (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner et al. or Anderson et al. and in further view of Allen et al. (Exp. Biol. Med. 226:498, 2001) or Olsen et al. (Lancet 339: 1003, 1992).

Claims 77 and 78 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt *et al.* (WO 94/17405) in view of Johnson *et al.* (NEJM 293: 675, 1975), Meis *et al.* (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) and in further view of Weiner *et al.* or Anderson *et al.* and in further view of Allen *et al.* (Exp. Biol. Med. 226:498, 2001) or Olsen *et al.* (Lancet 339: 1003, 1992). For all the reasons stated above, Leavitt *et al.*, Johnson *et al.*, Meis *et al.*, Keirse, Weiner *et al.* or Anderson *et al.*, Allen, or Olsen do not teach or suggest, either alone or in combination, a method of screening and treating a subject who is asymptomatic for preterm or imminent delivery by administering a progestational agent as described in independent claim 67 (from which claims 77 and 78 depend). Without this teaching, the references cited by the Examiner are insufficient to show obviousness. Therefore, the Appellants respectfully requests that the rejection of claim 77 and 78 under 35 U.S.C. §103, be reversed.

CONCLUSION

In light of the above arguments, Appellant respectfully submits that the cited references do not anticipate nor render obvious the claimed invention. More specifically, Appellants' claims recite novel physical features which patentably distinguish over any and all references under 35 U.S.C. §§ 112 and 103. As a result, a decision by the Board of Patent Appeals and Interferences reversing the Examiner and directing allowance of the pending claims in the subject application is respectfully solicited.

Dated: 3/26/2009

Respectfully submitted,

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APPENDIX A: PENDING CLAIMS

1-66 (canceled)

67. A method of screening and treating a subject, comprising: a) obtaining a sample from a subject who is asymptomatic for preterm or imminent delivery; b) detecting a fetal restricted antigen in said sample from said subject and assessing whether the level of fetal restricted antigen is indicative of a risk of preterm or imminent delivery; and c) if the level of fetal restricted antigen is indicative of the risk, administering a progestational agent to the subject, whereby delivery is delayed.

68. The method of claim 67, wherein, wherein the sample contains a body fluid or a swab of the posterior fornix, the cervical canal, the ectocervix and/or the external cervical os.

69. The method of claim 67, wherein a level indicative of the risk is above a minimum threshold amount.

70. The method of claim 67, wherein a level indicative of the risk is below a maximum threshold amount.

71. The method of claim 67, wherein the progestational agent is administered after the start of fetal organogenesis.

72. The method of claim 67 wherein the sample is obtained after about 12 weeks gestation.

73. The method of claim 67, wherein the sample is obtained after about 16 weeks gestation.

74. The method of claim 67 wherein the sample is obtained after about 20 weeks gestation.

75. The method of claim 67, wherein the administration of the progestational agent is stopped at about 36 weeks of gestation or at the onset of spontaneous labor.

76. The method of claim 67, wherein the fetal restricted antigen is fetal fibronectin.

77. The method of claim 67, wherein the progestational agent comprises at least one omega-3 fatty acid or a derivative thereof.

78. The method of claim 77, wherein the progestational agent comprises docosahexaenoic acid.

79. The method of claim 67, wherein the progestational agent is a progesterone-related agent.

80. The method of claim 79, wherein the progesterone-related agent is 17-.alpha.-hydroxyprogesterone or 17-.alpha.-hydroxyprogesterone caproate.

81. The method of claim 67, wherein the therapeutically effective amount of the progestational agent comprises at least about 100 mg/week of the progestational agent.

82. The method of claim 67, wherein the progestational agent is administered orally, by intramuscular injection, transdermally, or intranasally.

83. The method of claim 67, further comprising the step of: if the level of fetal restricted antigen is not indicative of a risk of preterm or imminent delivery, repeating at intervals at least one day apart the steps of detecting fetal restricted antigen in the sample and assessing whether the level of fetal restricted antigen is indicative of the risk; wherein if the level of fetal restricted antigen is indicative of the risk, administering a progestational agent to the subject, whereby delivery is delayed.

84. The method of claim 76, wherein the level indicative of the risk is a minimum threshold value of about 50 ng/mL.

85. The method of claim 76, wherein the sample is obtained from the posterior fornix.

86. The method of claim 76, wherein the sample is obtained from the cervical os.

87. The method of claim 76, wherein the level of fetal fibronectin is determined by the steps of: a) contacting the sample with an anti-(fetal fibronectin) antibody for a time sufficient to permit antigen-antibody binding to occur; b) contacting the sample with an insoluble support, to which anti-fibronectin antibody is adhered, for a time sufficient to permit antigen-antibody binding to occur; and c) detecting anti-(fetal fibronectin) antibody on the insoluble support.

88. The method of claim 87, wherein material from the sample is contacted with the insoluble support in a region of the insoluble support that contains mobilizable anti-(fetal fibronectin) antibody.

89. The method of claim 87, wherein the anti-(fetal fibronectin) antibody is conjugated to a physically detectable label.

90. The method of claim 87, wherein the step of detecting anti-(fetal fibronectin) antibody comprises the steps of: a) contacting the insoluble support with a labeled antibody which binds selectively with the anti-(fetal fibronectin) antibody; and b) detecting the label on the

insoluble support.

91. The method of claim 76, wherein the level of fetal fibronectin is determined by the steps of: a) contacting the sample with an anti-fibronectin antibody for a time sufficient to permit antigen-antibody binding to occur; and b) detecting formation of an antibody-antigen complex.

92. The method of claim 91, wherein the step of detecting formation of an antibody-antigen complex further comprises the steps of: c) contacting the sample with an insoluble support comprising an immobilized an anti-(fetal fibronectin) antibody under conditions, whereby fetal fibronectin in the sample binds to the antibody; and d) detecting the anti-fibronectin antibody on the insoluble support.

93. The method of claim 91, wherein the anti-fibronectin antibody comprises a detectable label.

94. The method of claim 93, wherein the step of detecting the anti-fibronectin antibody comprises the steps of: e) contacting the insoluble support with a labeled antibody that binds selectively with the anti-fibronectin antibody; and f) detecting the label on the insoluble support.

APPENDIX B: EVIDENCE

NONE

APPENDIX C: RELATED PROCEEDINGS

NONE